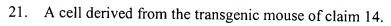
## **CLAIMS**

## We claim:

- 1. A targeting construct comprising:
  - (a) a first polynucleotide sequence homologous to at least a first portion of a PERK gene;
  - (b) a second polynucleotide sequence homologous to at least a second portion of the PERK gene; and
  - (c) a selectable marker.
- 2. A method of producing a targeting construct, the method comprising:
  - (a) providing a first polynucleotide sequence homologous to at least a first portion of a PERK gene;
  - (b) providing a second polynucleotide sequence homologous to at least a second portion of the PERK gene;
  - (c) providing a selectable marker; and
  - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
- 3. A cell comprising a disruption in a PERK gene.
- 4. The cell of claim 3, wherein the cell is a murine cell.
- 5. The cell of claim 4, wherein the murine cell is an embryonic stem cell.
- 6. A non-human transgenic animal comprising a disruption in a PERK gene.
- 7. The non-human transgenic animal of claim 6, wherein the transgenic animal is a mouse.
- 8. A cell derived from the transgenic mouse of claim 7.
- 9. A method of producing a transgenic mouse comprising a disruption in a PERK gene, the method comprising:
  - (a) introducing the targeting construct of claim 1 into a cell;
  - (b) introducing the cell into a blastocyst;
  - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
  - (d) breeding the chimeric mouse to produce the transgenic mouse.

- 10. A method of identifying an agent that modulates the expression or function of a PERK gene, the method comprising:
  - (a) providing a non-human transgenic animal comprising a disruption in a PERK gene;
  - (b) administering an agent to the non-human transgenic animal; and
  - (c) determining whether the expression or function of the disrupted PERK gene in the non-human transgenic animal is modulated.
- 11. A method of identifying an agent that modulates the expression or function of a PERK gene, the method comprising:
  - (a) providing a cell comprising a disruption in a PERK gene;
  - (b) contacting the cell with an agent; and
  - (c) determining whether the expression or function of the PERK gene is modulated.
- 12. The method of claim 11, wherein the cell is derived from the non-human transgenic animal of claim 6.
- 13. An agent identified by the method of claim 10 or claim 11.
- 14. A transgenic mouse comprising a disruption in a PERK gene, wherein there is no significant expression of the PERK gene in the transgenic mouse.
- 15. A transgenic mouse comprising a homozygous disruption in a PERK gene, wherein the transgenic mouse exhibits a perinatal lethality.
- 16. A transgenic mouse comprising a homozygous disruption in a PERK gene, wherein the transgenic mouse exhibits a congenital abnormality.
- 17. The transgenic mouse of claim 16, wherein the congenital abnormality comprises hydrocephaly.
- 18. The transgenic mouse of claim 16, wherein the transgenic mouse exhibits an abnormality in an organ selected from the group consisting of lung, heart, pancreatic gland, stomach and liver.
- 19. A transgenic mouse comprising a heterozygous disruption in a PERK gene, wherein the transgenic mouse exhibits an increased susceptibility to seizure.
- 20. The transgenic mouse of claim 19, wherein the mouse exhibits seizure-like responses at a lower dose of Metrazol, relative to a wild-type mouse.



- 22. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a PERK gene, the method comprising:
  - (a) administering an agent to a transgenic mouse comprising a disruption in a PERK gene; and
  - (b) determining whether the agent ameliorates at least one of the following phenotypes: a perinatal lethality, a congenital abnormality, or an increased susceptibility to seizure.
- 23. An agent identified by the method of claim 22
- 24. An agonist or antagonist of PERK.